

REMARKS

Claims 1-23 were pending in the present application, claims 1-5, 9, 11,12, 16, 21 and 22 were under examination, and claims 6-8, 10, 13-15, 17-20 and 23 stood withdrawn. In this paper, claims 12, 16, 21 and 22 are amended and claims 6-11, 13-15, 17-20 and 23 are cancelled without prejudice to Applicants' right to pursue the cancelled subject matter in one or more related divisional, continuation, and/or continuation-in-part applications. Thus, following entry of the present amendment, claims 1-5, 12, 16, 21 and 22 are pending and under consideration.

I. THE AMENDMENTS TO THE CLAIMS

The present paper presents an amendment to claims 12, 16, 21, and 22. The amendments to the claims are fully supported by the application as filed and therefore introduce no new matter.

In particular, support for the amendments to claims 16 and 22 may be found, for example, in claims 16 and 22 as filed. Support for the amendment to claim 21 may be found, for example, in claim 1 as filed. Claim 12 has been amended to depend from claim 5.

As the amendments to the claims are fully supported by the application as filed, these amendments introduce no new matter. Entry of the amendments to the claims is therefore respectfully requested under 37 C.F.R. § 1.111.

II. THE REJECTION OF CLAIM 21 FOR OMITTING ESSENTIAL STEPS SHOULD BE WITHDRAWN

Claim 21 stands rejected under 35 U.S.C. § 112, second paragraph, as the claim allegedly omits essential steps, such omission amounting to a gap between the steps. In particular, the PTO argues that the preamble recites a method to determine the status of cancer, but the active step of the method does not accomplish the purpose set out in the preamble.

Without acquiescing to the propriety of the rejection, Applicants believe the rejection is moot in view of the amendment to claim 21. Accordingly, Applicants respectfully submit that the rejection of claim 21 for omitting essential steps under 35 U.S.C. § 112, second paragraph is moot and respectfully request its withdrawal.

**III. THE REJECTION OF CLAIMS 1, 2, 5, 9, 11 AND 12
AS ANTICIPATED SHOULD BE WITHDRAWN**

Claims 1, 2, 5, 9, 11 and 12 stand rejected as anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 5,888,746 (the '746 patent). In particular, the PTO asserts that the '746 patent discloses a method for diagnosis or prognosis of a cancer that comprises "detecting an intracellular complex, protein tyrosine phosphat[as]e alpha (PTP α), in a sample from a subject, comparing the level in the first sample with the level in a second sample from normal tissue, wherein the cancer is colorectal cancer and wherein any over expression is indicative that the first sample is from a cancerous tissue." Applicants respectfully traverse.

Claim 1 and dependent claims 2, 5 and 12 recite methods for determining disease status that comprise, *inter alia*, measuring amounts of one or more intracellular complexes. As defined in the instant specification, a "complex" refers to "an assemblage or aggregate of molecules in direct or indirect contact with one another." See the specification at page 11, lines 9-10. Thus, claim 1 recites a method that comprises measuring amounts of one or more intracellular assemblages or aggregates of molecules.

In contrast, the '746 patent discloses methods that comprise measurement of amounts of PTP α protein or m-RNA. Applicants note that while the family of PTPs include non-receptor and receptor like enzymes ('746, column 1, lines 52-55), PTP α consists of a single polypeptide chain ('746, column 2, lines 38-40), and thus is not an intracellular complex. Thus, the '746 patent teaches methods that rely on measurement of amounts of a particular molecule, not aggregates or assemblages of molecules. As such, the '746 patent fails to teach each and every element of the invention defined by claims 1, 2, 5 and 12, and thus cannot anticipate such claims. See *Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 68 USPQ2d 185 (Fed. Cir. 2003). With respect to claims 9 and 11, Applicants have canceled these claims, thus rendering their rejection moot. Accordingly, Applicants respectfully request that the rejection of claims 1, 2, 5, 9, 11 and 12 as anticipated by the '746 patent be withdrawn.

**IV. THE REJECTION OF CLAIMS 3, 4, AND 21
AS OBVIOUS SHOULD BE WITHDRAWN**

Claims 3, 4 and 21 stand rejected as obvious over the '746 patent in view of Masters and Fu, 2001, *J. Bio. Chem.* 276(48):45193-200 ("Masters and Fu"). In particular, the PTO contends that it would be obvious to substitute measurement of PTP α in a patient sample for diagnosis or prognosis of cancer, as taught by the '746 patent, with measurement of 14-3-3//BAD complexes because Masters and Fu teach that 14-3-3 binds to and inhibits the

pro-apoptotic protein BAD, and overexpression of 14-3-3 in a cancerous cell may be inhibiting the normal function of BAD and other pro-apoptotic proteins. Applicants respectfully traverse.

Independent claim 21, as amended, and dependent claims 3 and 4 each recite methods for determining a disease status of a patient that recite, *inter alia*, measuring amounts of one or more intracellular complexes. As discussed above, such intracellular complexes are defined to be “an assemblage or aggregate of molecules in direct or indirect contact with each other.” Neither the ’746 patent nor Masters and Fu, either alone or in combination, teach or suggest a method for determining the disease status of a patient that comprises measuring an amount of “an assemblage or aggregate of molecules in direct or indirect contact with each other.” While Masters and Fu suggest that inhibition of 14-3-3 may represent a useful therapeutic target for treatment of cancer (abstract), Masters and Fu neither teaches nor suggests measuring amounts of 14-3-3/BAD complexes as a method for determining a disease status of a patient. As such, the ’746 patent and Masters and Fu, either alone or in combination, fail to teach or suggest each and every element of the invention as presently claimed. As the combination of cited references fails to teach each and every element of the invention as claimed, Applicants respectfully submit that the claims are not obvious over the cited references. *See In re Gartside*, 53 USPQ2d 1769 (Fed. Cir. 2000).

Further, nothing in either the ’746 patent or Masters and Fu provides any motivation to modify the teachings of these documents to obtain the claimed invention. For example, no teaching of the ’746 patent suggests that amounts of an intracellular complex, rather than amounts of PTP α protein or mRNA, should be measured in the methods of the ’746 patent. Absent such motivation to modify the cited references, the PTO cannot establish *prima facie* obviousness of the claimed invention. *See In re Kotzab*, 55 USPQ2d 1316 (Fed. Cir. 2000). As such, for this additional reason, the rejection of claims 3, 4, and 21 as obvious over the ’746 patent in view of Masters and Fu should be withdrawn.

V. THE REJECTION OF CLAIMS 16 AND 22 AS OBVIOUS SHOULD BE WITHDRAWN

Claims 16 and 22 stand rejected as obvious over the ’746 patent in view of Masters and Fu and further in view of U.S. Patent No. 6,627,400 (the ’400 patent). In particular, the PTO contends that it would be obvious to apply the method of the ’400 patent for determining the population of surface membrane proteins to the method of the ’746 patent for measuring PTP α in a patient sample for diagnosis or prognosis of cancer, in combination with the 14-3-3/BAD complex of Masters and Fu. Applicants respectfully traverse.

Nothing in the '400 patent cures the deficiencies of either the '746 patent or Masters and Fu with respect to the measurement of one or more intracellular complexes, as discussed above. In particular, the '400 patent neither teaches nor suggests that amounts of intracellular complexes should be measured in any method for determining disease status. As none of the cited references, alone or in combination, teaches or suggests that amounts of intracellular complexes should be measured in such methods, the combination of cited references fails to teach each and every element of the invention as claimed. Thus, Applicants respectfully submit that claims 16 and 22 are not obvious over the cited references. *See In re Gartside*, 53 USPQ2d 1769 (Fed. Cir. 2000).

Further, nothing in the '400 patent provides any motivation to modify the teachings of the '400 patent, '746 patent, or Masters and Fu to obtain the claimed invention. For example, no teaching of the '400 patent suggests that amounts of an intracellular complex, rather than amounts of a surface membrane protein, should be measured in the methods of the '400 patent. Absent such motivation to modify the cited references, the PTO cannot establish *prima facie* obviousness of the claimed invention.

Finally, Applicants note for the record that Applicants do not admit that the '400 patent is prior art to the present application.

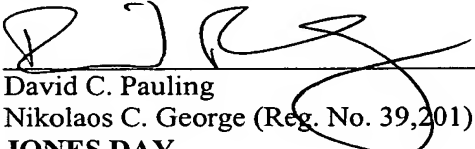
CONCLUSION

In view of the foregoing, Applicants respectfully submit that the present application is in condition for allowance and earnestly request an early indication of the same.

No fee is believed due with this response other than the fee for the extension of time for response. However, should the Commissioner determine otherwise, the Commissioner is hereby authorized to charge any required fee(s) to Jones Day Deposit Account No. 50-3013 (Order No. 949677-999138). A copy of this sheet is enclosed for such purpose.

Respectfully submitted,

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